

John Please  
SEARCH REQUEST FORM

25309

Requestor's

Name:

Brenda Coleman

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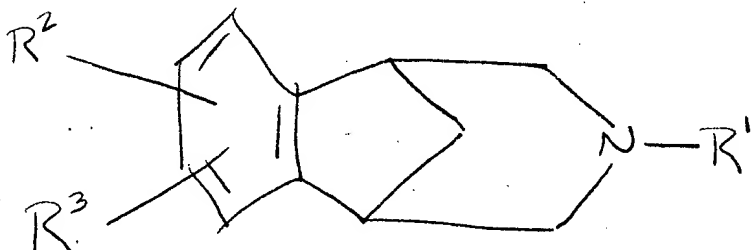
Date: Sept. 18, 2000

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Art Unit: 1624

## Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).



see claims 1, 11 and 14

Point of Contact:  
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## STAFF USE ONLY

PU 9-20-00  
Date completed: 9-20-00

Searcher: JOHN DANTZMAN

Terminal time: 35

Elapsed time:

CPU time:

Total time: 55

Number of Searches:

Number of Databases:

## Search Site

☒ STIC☐ CM-1☐ Pre-S

## Type of Search

☐ N.A. Sequence☐ A.A. Sequence☒ Structure☐ Bibliographic

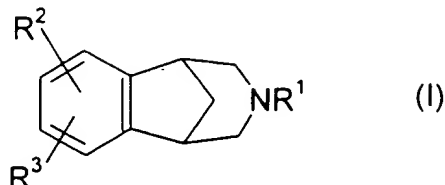
## Vendors

☒ IG Suite☒ STN☐ Dialog☐ APS☐ Geninfo☐ SDC☐ DARC/Questel☐ Other

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# CLAIMS

1. A compound of the formula



$R^1$  is hydrogen,  $(C_1-C_6)$ alkyl, unconjugated  $(C_3-C_6)$ alkenyl,  $XC(=O)R^{13}$  or  $-CH_2CH_2-O-$   $(C_1-C_4)$ alkyl;

10  $R^2$  and  $R^3$  are selected, independently, from hydrogen,  $(C_2-C_6)$ alkenyl,  $(C_2-C_6)$ alkynyl, hydroxy, nitro, amino, halo, cyano,  $-SO_q(C_1-C_6)$ alkyl wherein  $q$  is zero, one or two,  $(C_1-C_6)$ alkylamino-,  $[(C_1-C_6)alkyl]_2$ amino-,  $-CO_2R^4$ ,  $-CONR^5R^6$ ,  $-SO_2NR^7R^8$ ,  $-C(=O)R^{13}$ ,  $-XC(=O)R^{13}$ , aryl- $(C_0-C_3)$ alkyl- or aryl- $(C_0-C_3)$ alkyl-O-, wherein said aryl is selected from phenyl and naphthyl, heteroaryl- $(C_0-C_3)$ alkyl- or heteroaryl- $(C_0-C_3)$ alkyl-O-, wherein said heteroaryl is  
15 selected from five to seven membered aromatic rings containing from one to four heteroatoms selected from oxygen, nitrogen and sulfur, and  $X^2(C_0-C_6)alkoxy-(C_0-C_6)alkyl-$ , wherein  $X^2$  is absent or  $X^2$  is  $(C_1-C_6)alkylamino-$  or  $[(C_1-C_6)alkyl]_2$ amino-, and wherein the  $(C_0-C_6)alkoxy-(C_0-C_6)alkyl-$  moiety of said  $X^2(C_0-C_6)alkoxy-(C_0-C_6)alkyl-$  contains at least one carbon atom, and wherein from one to three of the carbon atoms of said  $(C_0-C_6)alkoxy-(C_0-C_6)alkyl-$  moiety may  
20 optionally be replaced by an oxygen, nitrogen or sulfur atom, with the proviso that any two such heteroatoms must be separated by at least two carbon atoms, and wherein any of the alkyl moieties of said  $(C_0-C_6)alkoxy-(C_0-C_6)alkyl-$  may be optionally substituted with from two to seven fluorine atoms, and wherein one of the carbon atoms of each of the alkyl moieties of said aryl- $(C_0-C_3)$ alkyl- and said heteroaryl- $(C_0-C_3)$ alkyl- may optionally be replaced by an oxygen, nitrogen  
25 or sulfur atom, and wherein each of the foregoing aryl and heteroaryl groups may optionally be substituted with one or more substituents, preferably from zero to two substituents, independently selected from  $(C_1-C_6)$ alkyl optionally substituted with from one to seven fluorine atoms,  $(C_1-C_6)alkoxy$  optionally substituted with from two to seven fluorine atoms, halo (e.g., chloro, fluoro, bromo or iodo),  $(C_2-C_6)$ alkenyl,  $(C_2-C_6)$ alkynyl, hydroxy, nitro, cyano, amino,  $(C_1-C_6)$ alkylamino-,  $[(C_1-C_6)alkyl]_2$ amino-,  $-CO_2R^4$ ,  $-CONR^5R^6$ ,  $-SO_2NR^7R^8$ ,  $-C(=O)R^{13}$  and  $-XC(=O)R^{13}$ ;

or  $R^2$  and  $R^3$ , together with the carbons to which they are attached, form a four to seven membered monocyclic, or ten to fourteen membered bicyclic, carbocyclic ring that can be saturated or unsaturated, wherein from one to three of the nonfused carbon atoms of said  
35 monocyclic rings, and from one to five of the carbon atoms of said bicyclic rings that are not part

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- 5 of the benzo ring shown in formula I, may optionally and independently be replaced by a nitrogen, oxygen or sulfur, and wherein said monocyclic and bicyclic rings may optionally be substituted with one or more substituents, preferably from zero to two substituents for the monocyclic rings and from zero to three substituents for the bicyclic rings, that are selected, independently, from (C<sub>1</sub>-C<sub>6</sub>) alkyl optionally substituted with from one to seven fluorine atoms, (C<sub>1</sub>-C<sub>6</sub>) alkoxy optionally substituted with from one to seven fluorine atoms, nitro, cyano, halo, (C<sub>2</sub>-C<sub>6</sub>) alkenyl, (C<sub>2</sub>-C<sub>6</sub>) alkynyl, hydroxy, amino, (C<sub>1</sub>-C<sub>6</sub>) alkylamino and [(C<sub>1</sub>-C<sub>6</sub>) alkyl]<sub>2</sub>amino, -CO<sub>2</sub>R<sup>4</sup>, -CONR<sup>5</sup>R<sup>6</sup>, -SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -C(=O)R<sup>13</sup> and -XC(=O)R<sup>13</sup>;

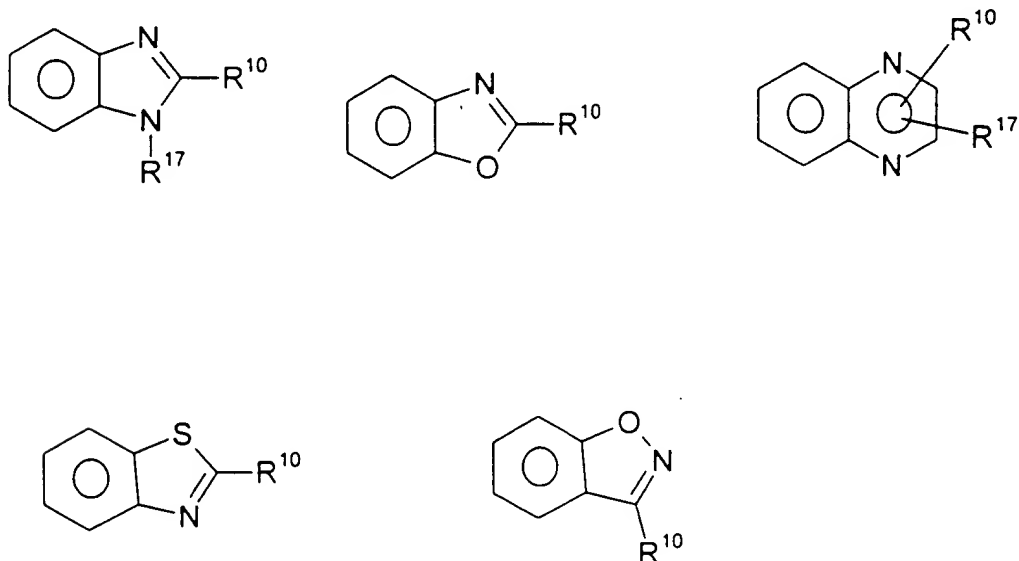
- 10 each R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>13</sup> is selected, independently, from hydrogen and (C<sub>1</sub>-C<sub>6</sub>) alkyl, or R<sup>5</sup> and R<sup>6</sup>, or R<sup>7</sup> and R<sup>8</sup> together with the nitrogen to which they are attached, form a pyrrolidine, piperidine, morpholine, azetidine, piperazine, N-(C<sub>1</sub>-C<sub>6</sub>) alkylpiperazine or thiomorpholine ring, or a thiomorpholine ring wherein the ring sulfur is replaced with a sulfoxide or sulfone; and

each X is, independently, (C<sub>1</sub>-C<sub>6</sub>) alkylene;

with the proviso that: (a) at least one of R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> must be the other than hydrogen,

- 20 and (b) when R<sup>2</sup> and R<sup>3</sup> are both hydrogen, R<sup>1</sup> cannot be hydrogen or methyl; or a pharmaceutically acceptable salt thereof;

2. A compound according to claim 1, wherein R<sup>2</sup> and R<sup>3</sup>, together with the benzo ring of formula I, form a bicyclic ring system selected from the following:



- 25 wherein R<sup>10</sup> and R<sup>17</sup> are selected, independently, from (C<sub>0</sub>-C<sub>6</sub>) alkoxy-(C<sub>0</sub>-C<sub>6</sub>) alkyl- wherein the total number of carbon atoms does not exceed six and wherein any of the alkyl moieties may optionally be substituted with from one to seven fluorine atoms; nitro, cyano, halo,

5 amino, (C<sub>1</sub>-C<sub>6</sub>)alkylamino-, [(C<sub>1</sub>-C<sub>6</sub>) alkyl]<sub>2</sub>amino-, -CO<sub>2</sub>R<sup>4</sup>, -CONR<sup>5</sup>R<sup>6</sup>, -SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -C(=O)R<sup>13</sup>,  
-XC(=O)R<sup>13</sup>, phenyl and monocyclic heteroaryl, wherein said heteroaryl is selected from five to  
seven membered aromatic rings containing from one to four heteroatoms selected from oxygen,  
nitrogen and sulfur,

3. A compound according to claim 1, wherein R<sup>2</sup> and R<sup>3</sup> do not, together with the  
10 benzo ring of formula I, form a bicyclic or tricyclic ring system.

4. A compound according to claim 1, wherein one or both of R<sup>2</sup> and R<sup>3</sup> are  
-C(=O)R<sup>13</sup> wherein R<sup>13</sup> is (C<sub>1</sub>-C<sub>6</sub>)alkyl.

5. A compound according to claim 1, wherein one of R<sup>2</sup> and R<sup>3</sup> is -COR<sup>13</sup> wherein  
R<sup>13</sup> is (C<sub>1</sub>-C<sub>6</sub>)alkyl or (C<sub>1</sub>-C<sub>3</sub>)alkyl optionally substituted with from one to seven fluorine atoms.

15 6. A compound according to claim 1, wherein one of R<sup>2</sup> and R<sup>3</sup> is CF<sub>3</sub>, fluoro,  
cyano or C<sub>2</sub>F<sub>5</sub>.

7. A pharmaceutical composition for use in reducing nicotine addiction or aiding in  
the cessation or lessening of tobacco use in a mammal, comprising an amount of a compound  
according to claim 1 that is effective in reducing nicotine addiction or aiding in the cessation or  
20 lessening of tobacco use and a pharmaceutically acceptable carrier.

8. A method for reducing nicotine addiction or aiding in the cessation or lessening  
of tobacco use in a mammal, comprising administering to said mammal an amount of a  
compound according to claim 1 that is effective in reducing nicotine addiction or aiding in the  
cessation or lessening of tobacco use.

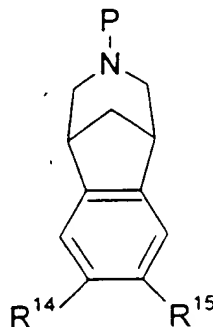
25 9. A pharmaceutical composition for treating a disorder or condition selected from  
inflammatory bowel disease (including but not limited to ulcerative colitis, pyoderma  
gangrenosum and Crohn's disease), irritable bowel syndrome, spastic dystonia, chronic pain,  
acute pain, celiac sprue, pouchitis, vasoconstriction, anxiety, panic disorder, depression, bipolar  
disorder, autism, sleep disorders, jet lag, amyotrophic lateral sclerosis (ALS), cognitive  
30 dysfunction, hypertension, bulimia, anorexia, obesity, cardiac arrhythmias, gastric acid  
hypersecretion, ulcers, pheochromocytoma, progressive supramuscular palsy, chemical  
dependencies and addictions (e.g., dependencies on, or addictions to nicotine (and/or tobacco  
products), alcohol, benzodiazepines, barbituates, opioids or cocaine), headache, stroke,  
traumatic brain injury (TBI), psychosis, Huntington's Chorea, tardive dyskinesia, hyperkinesia,  
35 dyslexia, schizophrenia, multi-infarct dementia, age related cognitive decline, epilepsy, including  
petit mal absence epilepsy, senile dementia of the Alzheimer's type (AD), Parkinson's disease  
(PD), attention deficit hyperactivity disorder (ADHD) and Tourette's Syndrome in a mammal.

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5 comprising an amount of a compound according to claim 1 that is effective in treating such disorder or condition and a pharmaceutically acceptable carrier.

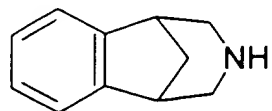
10 10. A method for treating a disorder or condition selected from inflammatory bowel disease (including but not limited to ulcerative colitis, pyoderma gangrenosum and Crohn's disease), irritable bowel syndrome, spastic dystonia, chronic pain, acute pain, celiac sprue, pouchitis, vasoconstriction, anxiety, panic disorder, depression, bipolar disorder, autism, sleep disorders, jet lag, amyotrophic lateral sclerosis (ALS), cognitive dysfunction, hypertension, bulimia, anorexia, obesity, cardiac arrhythmias, gastric acid hypersecretion, ulcers, pheochromocytoma, progressive supramuscular palsy, chemical dependencies and addictions (e.g., dependencies on, or addictions to nicotine (and/or tobacco products), alcohol, benzodiazepines, barbituates, opioids or cocaine), headache, stroke, traumatic brain injury (TBI), psychosis, Huntington's Chorea, tardive dyskinesia, hyperkinesia, dyslexia, schizophrenia, multi-infarct dementia, age related cognitive decline, epilepsy, including petit mal absence epilepsy, senile dementia of the Alzheimer's type (AD), Parkinson's disease (PD), attention deficit hyperactivity disorder (ADHD) and Tourette's Syndrome in a mammal, comprising administering  
20 to a mammal in need of such treatment an amount of a compound according to claim 1 that is effective in treating such disorder or condition.

11. A compound of the formula



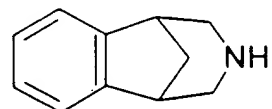
25 wherein P is hydrogen, methyl, COOR<sup>16</sup> wherein R<sup>16</sup> is (C<sub>1</sub>-C<sub>6</sub>)alkyl, allyl or 2,2,2-trichloroethyl; -C(=O)NR<sup>5</sup>R<sup>6</sup> wherein R<sup>5</sup> and R<sup>6</sup> are defined as in formula I above; -C(=O)H, -C(=O)(C<sub>1</sub>-C<sub>6</sub>)alkyl wherein the alkyl moiety may optionally be substituted with from 1 to 3 halo atoms, preferably with from 1 to 3 fluoro or chloro atoms; benzyl, t-butoxycarbonyl (t-Boc) or trifluoroacetyl, and R<sup>14</sup> and R<sup>15</sup> are selected, independently, from hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl optionally substituted with from one to seven fluorine atoms; -C(=O)(C<sub>1</sub>-C<sub>6</sub>)alkyl, cyano,  
30 hydroxy, nitro, amino, -O(C<sub>1</sub>-C<sub>6</sub>)alkyl and halo; with the proviso that R<sup>14</sup> and R<sup>15</sup> can not both be hydrogen when P is hydrogen or methyl.

- 5                    12. A method for reducing nicotine addiction or aiding in the cessation or lessening of tobacco use in a mammal, comprising administering to said mammal an amount of a compound comprising an amount of a compound of the formula



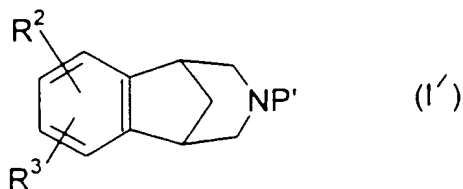
or a pharmaceutically acceptable salt thereof, that is effective in reducing nicotine  
10 addiction or aiding in the cessation or lessening of tobacco use.

13. A method for treating a disorder or condition selected from inflammatory bowel disease (including but not limited to ulcerative colitis, pyoderma gangrenosum and Crohn's disease), irritable bowel syndrome, spastic dystonia, chronic pain, acute pain, celiac sprue, pouchitis, vasoconstriction, anxiety, panic disorder, depression, bipolar disorder, autism, sleep  
15 disorders, jet lag, amyotrophic lateral sclerosis (ALS), cognitive dysfunction, hypertension, bulimia, anorexia, obesity, cardiac arrhythmias, gastric acid hypersecretion, ulcers, pheochromocytoma, progressive supramuscular palsy, chemical dependencies and addictions (e.g., dependencies on, or addictions to nicotine (and/or tobacco products), alcohol, benzodiazepines, barbituates, opioids or cocaine), headache, stroke, traumatic brain injury (TBI),  
20 psychosis, Huntington's Chorea, tardive dyskinesia, hyperkinesia, dyslexia, schizophrenia, multi-infarct dementia, age related cognitive decline, epilepsy, including petit mal absence epilepsy, senile dementia of the Alzheimer's type (AD), Parkinson's disease (PD), attention deficit hyperactivity disorder (ADHD) and Tourette's Syndrome in a mammal, comprising administering to a mammal in need of such treatment an amount of a compound of the formula



25 or a pharmaceutically acceptable salt thereof;  
that is effective in treating such disorder or condition.

14. A compound of the formula



30 wherein  $R^2$  and  $R^3$  are defined as in claim 1; and  $P'$  is  $\text{COOR}^{16}$  wherein  $R^{16}$  is allyl, 2,2,2-trichloroethyl or  $(\text{C}_1\text{-C}_6)\text{alkyl}$ ;  $-\text{C}(=\text{O})\text{NR}^5\text{R}^6$  wherein  $R^5$  and  $R^6$  are defined as in claim 2;

- 5 -C(=O)H, -C(=O)(C<sub>1</sub>-C<sub>6</sub>)alkyl wherein the alkyl moiety may optionally be substituted with from 1 to 3 halo atoms, preferably with from 1 to 3 fluoro or chloro atoms; benzyl, or t-butoxycarbonyl (t-Boc).

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I based structure search on a dictionary search in the registry file.

I searched for the set that has

C6/es = Benzene No fusion

C6/ess = benzene with fusion allowed

C5/es = cyclopentane No fusion

C5/ess = cyclopentane with fusion allowed

NC5/es = piperidine No fusion

NC5/ess = piperidine with fusion allowed

S = Same ring system

L18  $\Rightarrow$   $\begin{array}{ccc} \text{benzene} & \text{cyclopentane} & \text{piperidine} \\ \downarrow & \downarrow & \downarrow \\ \text{C6/ess} & \text{C5/ess} & \text{NC5/ess} \\ \uparrow & \uparrow & \\ \text{allows} & \text{Same ring} & \\ \text{fusion} & \text{system} & \end{array}$

I used this for a substructure search  
John D.